

**Remarks:**

Claims 1, 6 and 9 are rejected under 35 U.S.C. §112, first paragraph as containing subject matter not enabled by the specification. Applicants contend that the claims are directed to a range of polypeptides that require no undue experimentation for a skilled artisan to make and use. First, the claimed polypeptides are derivatives of SEQ ID NO:1, wherein substitutions are made within the F2a and F2c regions of SEQ ID NO:1. The F2a region of SEQ ID NO:1 is identified as corresponding to amino acids 60-67 of that sequence, and the F2c region is identified as corresponding to amino acids 77-83 of that sequence (see Figure 1, and accompanying text). The substitution in region F2a is defined as comprising from 4 to 8 amino acids and the substitution in region F2c is defined as comprising 7 to 8 amino acids. The amino acids from the F2a and F2c regions of SEQ ID NO:1 are, according to the claims, to be substituted with the corresponding amino acids of SEQ ID NO:4. Examples of such substitutions are also provided in the specification, and working examples are provided in the Examples. Figure 1 shows an alignment of the sequences of the four GDNF family neurotrophic factors, and identifies the F2a and F2c regions of each. Thus, the specification provides ample guidance for constructing the claimed polypeptides. Also, the Examples provide a method by which one skilled in the art may assay the polypeptides that fit the structural limitations of the claims to determine whether they possess the functional limitations of the claims. Construction of the various polypeptides, with amino acids from the F2a and F2c regions of SEQ ID NO:1 being replaced with the corresponding amino acids from SEQ ID NO:4, is a matter of routine experimentation for the skilled artisan, and performing the assay described in the examples to ascertain whether a particular polypeptide possesses the functional limitations of the claims is also a matter of routine experimentation. None of the experimentation required to make and use the claimed polypeptides can be considered undue experimentation given the extensive guidance provided by the claims themselves and the specification. Further, the specification provides a working example of the claimed polypeptide, where four amino acids from the F2a region of a persephin polypeptide have been substituted with the corresponding 4 amino acids from GDNF, and seven amino acids in the F2c region of

persephin have been substituted with the corresponding seven amino acids from GDNF, and where that polypeptide has been shown to possess the claimed function.

Claims 1 and 6-9 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Specifically, the Office states that the claim language is confusing in that claim 1 is directed to SEQ ID NO:1, further comprising substitutions. Please note the amendments to that claim above. Applicant has defined the claimed polypeptide as being a persephin polypeptide, with substitutions in the F2a and F2c regions, of that polypeptide. The F2a and F2c regions are identified with reference to SEQ ID NO:1. The substitutions are from the corresponding regions of SEQ ID NO:4. Thus, the claimed polypeptides comprise a persephin sequence, where the specifically identified amino acids have been replaced with the corresponding specific amino acids from SEQ ID NO:4. The claims are not, as the Office indicates, directed to SEQ ID NO:1. Thus, the claims are not indefinite.

Claim 7 has been amended to be in independent form, and claim 8 has been amended to depend from claim 7. Thus, the objections to those claims are now moot.

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, he is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,



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